REMARKS

Claims 13 and 15 have been amended to more clearly define the subject matter of the invention.

Support for the amendment to claim 13 can be found on page 5, lines 3-5; page 11, lines 1-3 and page 11, line 18 to page 12, line 4.

Support for the amendments to claim 15 can be found on page 9, lines 1-5 and in claim 13.

No new matter has been added.

Oath/Declaration

The Examiner indicates that it is unclear whether the Oath or Declaration is defective. She points to the discrepancy between the Oath or Declaration, which lists a United Kingdom application as 9210944.6, filed May 22, 1992, and the Application Data Sheet which references this United Kingdom application as 92109.44, filed May 22, 1992. Applicants include the face page of the priority document which clearly indicates that United Kingdom application 9210944.6 was filed on May 22, 1992. Applicants enclose a corrected Application Data Sheet listing this correct application number.

Objections

The Examiner has objected to claim 16, contending that it fails to further limit the subject matter of a previous claim. The Examiner notes that independent claim 13 requires that the anti-idiotypic antibody product bind a breast cancer cell line and that dependent claim 16 reads broadly on cancer cells of epithelial origin. Applicants have amended claim

13 to indicate that the anti-idiotypic antibody must be bind to at least a Lewis Y carbohydrate expressing cell of a Lewis Y positive human breast cell line. Applicants also amended claim 15 to indicate that an immune response is produced against any Lewis Y carbohydrate-expressing cells. Applicants respectfully submit that the objection is overcome based on this amendment.

Rejections Under 35 USC § 102

The Examiner has rejected claims 13-19, 23 and 28 as being anticipated by Loibner et al. The Examiner's position is that the antibodies disclosed in the Loibner reference would act in the same manner as those claimed, i.e. by retaining equivalent inhibition capacity and producing immune response against Lewis Y carbohydrate-expressing cells. Applicants respectfully traverse.

Applicants submitted a Declaration by Dr. Hans Loibner in a Preliminary Amendment filed February 18, 2003. In this Declaration, Dr. Loibner states that the Loibner reference only teaches producing a mixture of antibodies and does not teach the instant invention. In order to accentuate this difference, Applicants have amended claim 13 to indicate that it is an isolated monoclonal murine internal image anti idiotypic antibody that is the subject of the invention. Claim 15 has also been amended to indicate that each monoclonal antibody present in the pharmaceutical composition must have an inhibition capacity of more than 95% in terms of inhibition of binding of BR55-2 murine Ig2a to at least a Lewis Y carbohydrate positive expressing cell of a Lewis Y human breast cancer cell.

In addition, Applicants present the results of experiments that indicate that not all of the isolated antibodies produced from several hybridoma cell lines are internal image

antibodies that show more than 95% inhibition in terms of binding BR55-2 murine IgG2a to a Lewis Y positive human breast cancer cell line and at a concentration of less than or equal to a ten fold excess of Ab2 to Ab1. These results are presented in the enclosed Declaration by Dr. Günter Waxenecker. In view of the above, Applicants request reconsideration and removal of the rejection.

Rejections Under 35 USC § 103

The Examiner has rejected claims 13-19, 23 and 28 as being obvious over US Patent No. 4,971,792 ('792; Potocnjak). The Examiner contends that the '792 patent teaches monoclonal antibodies BR55-2 which bind to malignant cells expressing one or more determinants such as Y-6 and B-7-2. The Examiner acknowledges that the patent does not teach monoclonal murine internal anti-idiotypic antibodies to the said monoclonal antibodies designated as BR55-2. The Examiner, however, points to the statement made in the reference that other hybridomas secreting monoclonal antibodies with the specificity of the monoclonal antibodies of the '792 patent could be accomplished by a skilled artisan using the technique of anti-idiotypic screening. The Examiner contends that while Potocnjak does not describe the particulars of the screening criteria, there is no evidence that one would not obtain the anti-idiotypic antibody of the instant application using the technique of Potocnjak. The Examiner further contends that the antibodies obtained would intrinsically act in the same manner as those claimed in the instant invention, i.e. retain equivalent inhibition capacity and produce an immune response against Lewis Y carbohydrate-expressing cells. The Examiner states that the skilled artisan would have been motivated to do this with a reasonable expectation of success by the teaching in the

'792 patent as well as the fact that anti-idiotypic responses are complementary to antibody responses since they both play roles in regulating humoral and cell-mediated immunity. Applicants respectfully traverse.

Applicants first point out that Potocnjak et al. do not disclose or indicate a selection method for internal-image anti-idiotypic antibodies as described in the present application. Potocnjak et al. describe the inhibition of idiotype-anti-idiotype interaction for the detection of a parasite antigen. On page 1638, left column, lines 7-9, it is stated that the isolated 2D12 anti-idiotypic antibody is bound to an epitope of 3D11 close to or in its antigen-combining site. That is, the authors were unable to clearly state that the isolated 2D12 anti-idiotypic antibody is definitely an internal-image antibody. The instant invention, on the other hand, discloses a screening method for isolating anti-idiotypic antibodies that do not recognize the remaining constant regions of the $F(ab)_2$-fragment of a monoclonal antibody BR55-2 (ABL364) used for immunization but represent internal-image antibodies of unique inhibition capacity.

Applicants again point to the enclosed Declaration by Dr. Waxenecker which shows that not all of the isolated antibodies from several hybridoma cell lines are internal image antibodies that have an inhibition capacity of more than 95% in terms of inhibition of binding BR55-2 murine IgG2a to at least a Lewis Y positive human breast cancer cell line. These results are summarized in Table 4 of the Declaration. As you can see, not all of the antibodies obtained by the immunization procedure have the capacity to sufficiently inhibit Lewis Y binding of the Lewis Y specific antibody 880-365 (BR55-2/mIgG2a). For example, antibodies from clone 3C12 have no capacity to inhibit LeY binding of the LeY specific

antibody 880-365 while antibodies from clone 4F2 show an inhibition capacity of 75% and products from clone 2F11 exhibit 96% inhibition capacity.

Potacnjak et al. do not describe the criteria of the screen needed. Without these criteria, one cannot guarantee obtaining an antibody suitable for medical purposes and being an internal-image anti-idiotypic antibody. In view of the above and the experimental evidence submitted in Dr. Waxenecker's Declaration, Applicants respectfully request reconsideration and removal of the rejection.

In view of the above remarks, all of the claims remaining in the case are submitted as defining non-obvious, patentable subject matter.

Pursuant to 37 C.F.R. §§ 1.17 and 1.136(a), the Applicant respectfully petitions for a three (3) month extension of time for filing a response in connection with the present application and the required fee of $950.00 is attached hereto.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Leoanrd R. Svensson (Reg. No. 30,330) at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

BIRCH, STEWART, KOLASCH & BIRCH, LLP

Certificate of Transmission
I hereby Certify that this correspondence is being facsimile transmitted to the Patent and Trademark Office:
On July 16, 2004
Date
Signature
Sandra B. Pirlo
Typed or printed name of person signing certificate

#47,604

By _____
for Leonard R. Svensson, #30,330

P.O. Box 747
Falls Church, VA 22040-0747
(703) 205-8000

LRS/SWG/sbp
4518-0101P

Attachment(s): Declaration Under 37 CFR § 1.132
Supplemental Application Data Sheet

(Rev. 02/12/2004)